Glass and Ceramics, Vol. 67, Nos. 11 – 12, March, 2011 (Russian Original, Nos. 11 – 12, November – December, 2010)

BIOMATERIALS

UDC 661.842.455:61:663.3

BIOCOMPOSITE MATERIAL BASED ON DICALCIUM PHOSPHATE DIHYDRATE

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Translated from *Steklo i Keramika*, No. 11, pp. 23 – 26, November, 2010.

The results of wet two-stage synthesis of tricalcium phosphate followed by high-temperature treatment are reported. The effect of incorporating tricalcium silicate and alkaline silicate glasses in formation of biocomposite materials based on dicalcium phosphate dihydrate (DCPD) was examined. It was found that use of the bioactive glass 50S25N5P in the amount of up to 10% of the mass content increases the compressive strength and pH to a physiologically safe level in the composite material in comparison to unmodified DCPD. The composite obtained ensures formation of osteoid tissue for 30 days.

Key words: biocomposite, dicalcium phosphate dihydrate, bioactive glass, β-tricalcium phosphate.

Implantation materials made of bioactive glass and glass ceramics are used in practice in osteoplastic surgery to reduce defects of complex shapes. Attaching and fitting the implant snugly in the bone matrix is the key problem in implanting them: in most cases, the implant is fixed with titanium plates, screws, and pins and gaps are filled with bone chips. Using titanium attachment systems disturbs the integrity of the prosthetic material and causes dangerous stresses in its bulk. An alternative solution is to use bone cements made of hydroxyapatite (HA) $Ca_{10}(PO_4)_6(OH)_2$ and dicalcium phosphate dihydrate (DCPD) $CaHPO_4 \cdot 2H_2O$; in attaching bone fragments with the implant material, they ensure a tight fit. The advantage of these compositions is the possibility of injecting them through a syringe, which atraumatically increases the density of bone tissue, for example, the bodies of vertebrae damaged by osteoporosis [1, 2].

We attempted to create a composite material from DCPD and resorbable, easily hydrated silicate glasses to increase the porosity of cement stone and regulate the pH and initial strength.

We know that dicalcium phosphate dihydrate is one of the most soluble calcium phosphates in physiological medium with pH = 7.2 – 7.4. The solubility of DCPD ($PR = 10^{-6.63}$) is higher than the solubility of HA ($PR = 10^{-117.2}$), and the biodegradation rate is comparable to the rate of regeneration of bone tissue.

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The high-temperature form of tricalcium phosphate — β-$Ca_3(PO_4)_2$ (β-TCP), obtained by precipitation of calcium nitrate and ammonium hydrophosphate from aqueous solutions with addition of ammonium hydroxide to maintain the pH at 6 – 7 according to the following reaction [3] is one of the components for obtaining DCPD

$$3Ca(NO_3)_2 + 2(NH_4)_2HPO_4 + 2NH_4OH = Ca_3(PO_4)_2 \cdot 2H_2O\downarrow + 6NH_4NO_3. \quad (1)$$

According to the XPA data, the reaction products are represented by a series of phases of variable composition (Fig. 1*a*). The filtered and dried residue is represented by β-TCP after heat treatment at $T = 1200$°C for 4 h (Fig. 1*b*). Synthesis of β-TCP is two-stage and ensures a 100% yield of the final product of the reactions.

The IR spectra of the β-$Ca_3(PO_4)_2$ obtained contains absorption bands corresponding to vibrations of PO_4^{3-} groups and Ca^{2+}. There are no vibrations of hydrophosphate HPO_4^{2-}, pyrophosphate PO_7^{4-} carbonate CO_3^{2-}, and hydroxyl OH^- groups, which indicates completion of dehydration and decarbonization reactions.

According to the findings of electron microscopic analysis, precipitated β-$Ca_3(PO_4)_2$ is represented by agglomerates 0.5 – 50 μm in size. After heat treatment, the tricalcium phosphate crystals are round and are no larger than 0.5 μm.

Dicalcium phosphate dihydrate was obtained by hydration of β-TCP and monocalcium phosphate (MCP) taken in

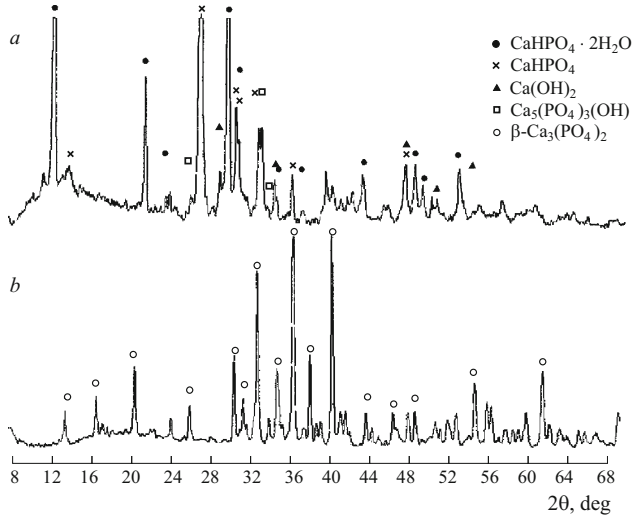

Fig. 1. X-ray pattern of tricalcium phosphate: *a*) initial; *b*) after heat treatment at 1200°C.

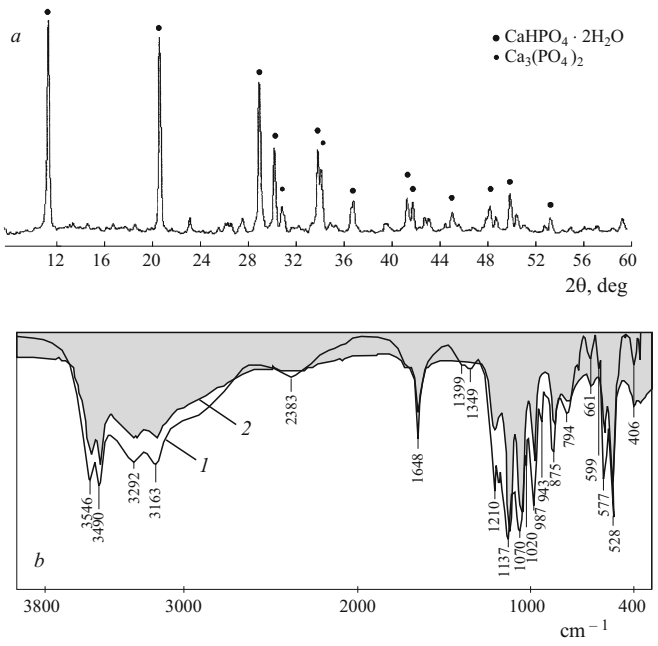

Fig. 2. X-ray pattern (*a*) and IR spectrum (*b*) of DCPD: *1*) DCPD obtained in the study; *2*) DCPD from Sadtler Inc. library data.

the amount of 60%[3] and 40%, respectively, according to the reaction

$$\beta\text{-}Ca_3(PO_4)_2 + Ca(H_2PO_4)_2 \cdot H_2O + 7H_2O \rightarrow 4CaHPO_4 \cdot 2H_2O. \quad (2)$$

DCPD crystallizes in the form of lamellar crystals whose physical coupling and intertwining give the cement stone strength. XPA identified a single-phase product of the composition of DCPD 24 h after the reaction (Fig. 2*a*). The IR spectra (Fig. 2*b*) contained vibrations of HPO_4^{3-}, CO_3^{2-}, and OH^- groups. The bands in the 1300 – 1700 and 2300 – 2450 cm^{-1} regions are characteristic of hydrophosphates and are considered combination bands forthese anions.

The dicalcium phosphate dihydrate obtained crystallized in the form of uniform prismatic crystals approximately 8 μm long and 2 μm wide (Fig. 3). The elemental composition obtained by microanalysis of different regions and points was the same. DCPD was characterized by porosity of $P \approx 40 – 45\%$, pore size of about 5 – 50 μm, pH = 3.3, and compressive strength of $\sigma_c = 15$ MPa.

The basic drawbacks of dicalcium phosphate dihydrate are the low pH, which can cause tissue burns and inflammatory reactions in the body.

To increase the pH of the physiological solution in contact with $CaHPO_4 \cdot 2H_2O$, alkaline calcium silicate and silicate glasses are added during synthesis:

– tricalcium silicate $3CaO \cdot SiO_2$ with 40 μm particles;

– liquid sodium glass $Na_2O \cdot mSiO_2 \cdot nH_2O$;

– 50S25N5P bioactive glass (composition, %: 50.0 SiO_2; 25.0 Na_2O; 20.0 CaO; 5.0 P_2O_5) with 120 – 200 μm particles.

The investigated additives are additional sources of silicon ions which are present in bone tissue in the amount of 17×10^{-4}% and participate in biological processes [4]. The silicon boosts cell activity; it increases output of type I collagen by the cells in the stage of formation of organic bone matrix (osteoid), and later in the mineralization stage, causes precipitation of calcium phosphates.

The amount of glasses added varied within the limits of 1 – 10% of the weight of the initial calcium phosphates.

The increase in the concentration of tricalcium silicate and liquid sodium glass decreased the compressive strength of the samples of dicalcium phosphate dihydrate. Hypothetically, this was due to incorporation of tricalcium silicate in the dicalcium phosphate dihydrate conglomerate in the first case and in the second, to formation of sodium glass films on the surface of particles of dicalcium phosphate dihydrate; in both cases, the structure of the DCPD stone formed is dis-

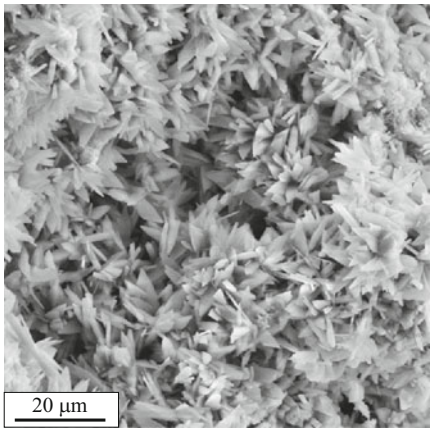

Fig. 3. Microstructure of dicalcium phosphate dihydrate.

[3] Here and below, mass content.

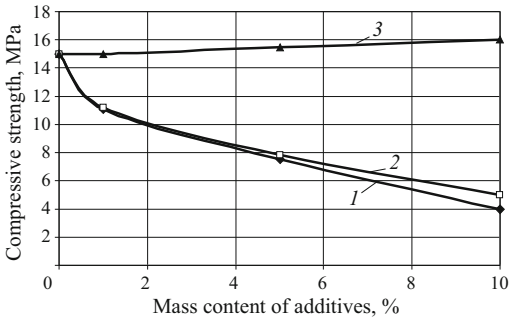

Fig. 4. Strength of DCPD composite materials as a function of mass content of additives: *1*) $3CaO \cdot SiO_2$; *2*) $Na_2O \cdot mSiO_2 \cdot nH_2O$; *3*) 50S25N5P.

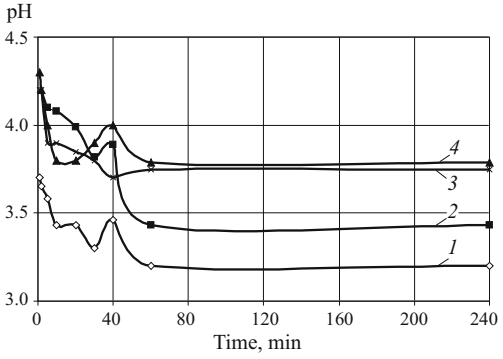

Fig. 5. Changes in pH of physiological solution as a function of holding time of DCPD composite materials in buffer solution with different additives: *1*) DCPD with no additives; *2*) 5% $3CaO \cdot SiO_2$; *3*) 10% 50S25N5P; *4*) 5% $Na_2O \cdot mSiO_2 \cdot nH_2O$.

turbed and the strength decreases (Fig. 4). The bioactive glass granules, on the contrary, increase the strength of the composite: when the β-TCP + MCP + 50S25N5P system was exposed to water, the glass underwent active hydration for the first 2 min with formation of active Si^{3+}–OH groups on the surface which acted as precursors of the DCPD crystallized in the system. The Si^{3+}–O–Ca^{-} chemical bonds formed in the system are stronger than P^{4+}–O–Ca^{-}, which increases the initial strength of the composite when glass is added in the amount of up to 10%. The initial strength for these materials is an important characteristic, since implant material, cement stone in particular, must stabilize bone fragments from the time it is introduced until it is resorbed. A composite material is formed with a calcium phosphate matrix and a bioresorbable glass filler. All of the additives used increase the pH of dicalcium phosphate dihydrate (Fig. 5).

Optical microscopy with magnification by 21 times was conducted for samples of DCPD and DCPD + 50S25N5P before and after buffering in DMEM for 14 days (Fig. 6). The results showed that this composite was characterized after buffering by a large difference in pore sizes: about 10 – 150 μm in comparison to samples of buffered DCPD: about 5 – 50 μm. In hydration of bioactive glass granules, a local increase in the pH above 7 hypothetically takes place, and

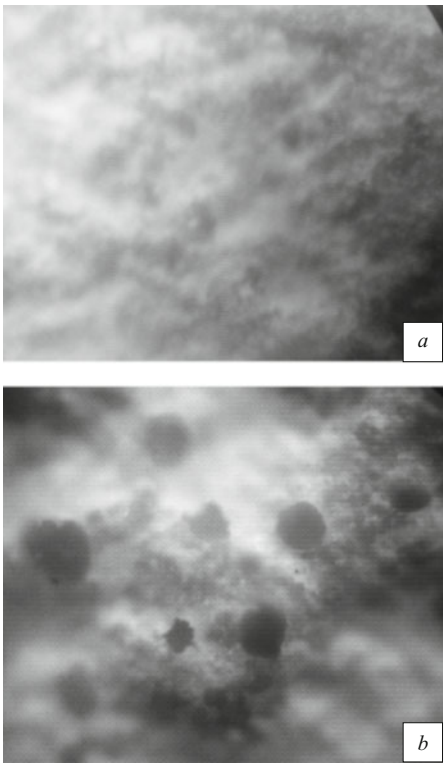

Fig. 6. Optical photographs of samples of DCPD + 50S25N5P: *a*) initial; *b*) after holding in buffer solution for 14 days.

the solubility of DCPD in this region will thus increase. After implantation of biocomposite DCPD + 50S25N5P in bone tissue, this will cause formation of a bimodal pore structure in the resorption stage and improve penetration of cells and formation of bone tissue in the bulk of the material.

The biocompatibility, resorbability, and osseointegration of the composite material made from dicalcium phosphate dihydrate with bioglass granules were investigated on experimental models of ectopic osteogenesis and orthotopic implantation with placement of the cement composite investigated in the intramuscular pocket or intraosseous perforation (in rats).

The composite material obtained exhibited elevated biocompatibility and osseointegration. Resorption of the biocomposite and formation of osteoid tissue were observed in the animals 30 days after implantation.

The results of the studies show that incorporation of 50S25N5P bioactive glass in the composite in the amount of up to 10% increased the strength characteristics to 16 MPa and the pH to 3.8 in comparison to the initial DCPD and ensured formation of a bimodal pore structure on holding in buffer solution, good impregnability, and penetration of the material in bone cells. Samples of the composite were resorbed and caused formation of osteoid tissue in the region of the defect. The glass ceramic materials can be used both for attaching bone fragments and installation of glassy and glass ceramic implants and in formation of cold-hardened implants. This allows incorporating titanium reinforcing ele-

ments in large and complexly shaped implants without risking their oxidation, which takes place in reinforcement of implants obtained by sintering.

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